Claims

We claim:

1. A polypeptide comprising a human interleukin-2 mutein numbered in accordance with wild-type IL-2 wherein said human IL-2 is substituted at at least one of positions 20, 88 or 126, whereby said mutein preferentially activates T cells over Natural Killer cells.

2. The human IL-2 mutein of claim 1 wherein position 20 is substituted relative to wild-type.

3. The human IL-2 mutein of claim 2 wherein said position 20 is substituted with isoleucine.

4. The human IL-2 mutein of claim 2 wherein said position 20 is substituted with histidine.

5. The human IL-2 mutein of claim 1 wherein position 88 is substituted relative to wild-type.

6. The human IL-2 mutein of claim 6 wherein said position 88 is substituted with arginine.

7. The human IL-2 mutein of claim 5 wherein said position 88 is substituted with isoleucine.

8. The human IL-2 mutein of claim 5 wherein said position 88 is substituted with glycine.

9. The human IL-2 mutein of claim 1 wherein said position 126 is substituted relative to wild-type.

10. The human IL-2 mutein of claim 9 wherein said position 126 is substituted with aspartate.

11. The human IL-2 mutein of claim 9 wherein said position 126 is substituted with glutamate.

12. The human IL-2 mutein of claim 9 wherein said position 126 is substituted with leucine.

13. A pharmaceutical composition comprising a polypeptide of claim 1 in combination with a pharmaceutically acceptable carrier.

14. A polynucleotide comprising a DNA sequence encoding a human IL-2 mutein of claim 1 and degenerate variants thereof.

15. A prokaryotic host cell transformed with the polynucleotide of claim 14.

16. A vector comprising the polynucleotide of claim 14.

17. A method of treating a mammal afflicted with an IL-2 treatable condition by administering a therapeutically effective amount of a human IL-2 mutein of claim 1.

18. The method of claim 17 wherein said IL-2 treatable condition is selected from the group consisting of HIV, cancer including renal carcinoma and malignant melanoma, autoimmune disease, infectious disease, immune deficiency including SCID, or other therapeutic application requiring general stimulation of the immune system.

19. A method of selecting IL-2 muteins through evaluation in assays utilizing IL-2R$\alpha\beta\gamma$ in comparison with IL-2R$\beta\gamma$, wherein the activity of an IL-2 mutein is increased relative to wt IL-2 in one assay preferentially to the other.

20. The method of claim 19 wherein IL-2Rαβγ and IL-2Rβγ are the individual receptor subunit ectodomains in appropriate combination, and are used to measure directly the binding of IL-2 muteins to each receptor complex.

21. The method of claim 19 wherein the IL-2αβγ assay utilizes a response from an IL-2αβγ-bearing cell type, and the IL-2βγ assay utilizes a response from an IL-2βγ-bearing cell type.

22. The method of claim 21 wherein the IL-2αβγ-bearing cell is a PHA-blast, and the IL-2βγ-bearing cell is a NK cell.

23. The method of claim 22 where the assay is proliferation for both the IL-2αβγ-bearing cell type and the IL-2βγ-bearing cell type.